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Optimization of a Myeloid Cell Transfusion Strategy for Infected Neutropenic Hosts

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Background: Although granulocyte transfusion is a logical therapeutic option for neutropenic patients with refractory infections, significant technical barriers have prevented its wide-spread use.
Objectives: A novel phagocyte transfusion strategy has been developed based on activation/differentiation of a human myeloid cell line, HL-60.
Methods: To optimize the HL-60 transfusion system, varying durations of cell activation were compared, facile quality control markers were developed to track lot-to-lot variability, and the impact of low dose irradiation on cell function was determined.
Results: A three day period of activation resulted in increased cell viability and in vitro candidacidal capacity, but with slightly higher cell replication, compared to a seven day activation period. Cell viability and several facile flow cytometric measurements were accurate quality-control markers for HL-60 activation. In combination with activation, low-dose irradiation abrogated replication while sparing the HL-60 cells' candidacidal effects. Infusion of irradiated, activated HL-60 cells significantly improved survival of neutropenic, candidemic mice.
Conclusions: In summary, activated, irradiated HL-60 cells are microbicidal, have virtually no replicative capacity, and are safe and effective at protecting neutropenic mice against an otherwise 100% fatal candidal infection. With continued development, this strategy to recapitulate neutrophil functions has the potential to serve as an effective alternative to granulocyte transfusions.

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Analysis of the Role of [^{18}F] Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) Imaging in Early Diagnosis and Management of Invasive Mold Infections (IMIs)

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Background: Invasive mold infections (IMIs) are leading causes of mortality in severely immunocompromised patients. Early diagnosis of IMIs by conventional methods is challenging, and there is need for innovation in this area. Emerging evidence suggests that [^{18}F] fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging could be a useful tool in diagnosis and management of a range of opportunistic infections in immunocompromised patients.
Methods: We retrospectively evaluated the medical records of patients with probable or proven IMI (n = 13) who underwent FDG PET imaging around the time of their infection, at The University of Texas M.D. Anderson Cancer Center over a 5-year period (12/1999 to 4/2004). We additionally reviewed the available literature on FDG PET imaging in diagnosis and/or follow up of patients with IMIs (n = 9).
Results: We identified 22 patients with IMIs (15 definite, 7 probable). FDG PET imaging was performed for cancer staging in the majority (14/22 or 64%) of cases. Most patients had an underling malignancy (16/22 or 73%), primarily of haematological origin (12/16 or 75%), and typical risk factors for IMIs, including receipt of a significant dose of corticosteroids (14/22 or 46%), and severe neutropenia (4/22 or 18%). In 7 recipients of allogeneic HSCT most had developed active GVHD (6/7 or 86%). All IMIs were caused by either *Aspergillus* (16/22 or 73%) or *Zygomycetes* (6/22 or 27%) species. Pneumonia was the predominant manifestation of IMIs (17/22), whereas there were 4 cases of disseminated infection and 1 case of sinusitis.
The median day of FDG PET study in respect to IMI diagnosis was day 15 (range: day 26 to day 60). The median standardized uptake value SUV of lesions caused by IMIs was 3.7 (range: 0.9–11.8). In 16 eligible patients, FDG PET revealed an occult site of infection in 3 (19%) cases of disseminated IMIs (including 2 cases with CNS involvement) and was helpful in guiding antifungal treatment in 9 (56%) patients with IMI.
Conclusion: FDG PET imaging has the potential to become a useful tool for diagnosis of occult foci of disseminated IMIs and monitoring of antifungal treatment. However, prospective validation and analysis of cost effectiveness of FDG PET imaging in patients with IMIs is needed.